EXHIBIT E

NDA 20-235
NDA 20-882
NDA 21-129

Pfizer, Inc.
Attention: Manini Patel
Director, Worldwide Regulatory Affairs
235 E. 42nd Street 150/7/6
New York, NY 10017

Dear Ms. Patel:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Neurontin (gabapentin) Capsules, Neurontin (gabapentin) Tablets, and Neurontin (gabapentin) Oral Solution.

There is evidence that patients with epilepsy are at an elevated risk for suicidality (suicidal thinking and behavior) and completed suicide. Despite this elevated population risk, the concern has been raised that some anti-epileptic drugs (AEDs) may be associated with an increased risk of suicidality. Given the recent observation of suicidality as a drug-induced adverse effect in pediatric patients exposed to various antidepressants in placebo-controlled trials, there is interest in examining data from placebo-controlled trials of AEDs to assess for a similar effect. Based on our experience with the pediatric antidepressant trials, the Division of Neuropharmacological Drug Products (DNDP) has developed a standard approach for evaluating drug-induced suicidality. Thus, we ask that you utilize the approach we have outlined in this letter for evaluating "possibly suicide related" adverse events occurring in placebo-controlled trials for gabapentin.

We request that you identify the trials from your development program (regardless of whether the indication is approved or not) that meet the following criteria: placebo-controlled; parallel arm; short-term (up to six months); at least 30 patients total. Some trials in epilepsy may have utilized a subtherapeutic dose of a standard AED as a comparator arm. Those trials should be included (if they meet the other criteria described above) and the subtherapeutic comparator arm should be coded as a "low dose-placebo" (see variable list below).

Once we have agreed upon the list of trials upon which to focus this exploration, we ask that you utilize the following approach to identifying and further evaluating "possibly suicide related" adverse events occurring in these trials.

Search for "Possibly Suicide-Related" Adverse Events and Preparation of Narrative Summaries

Time Frame for "Possibly Suicide-Related" Adverse Events

This search should be strictly limited to adverse events that occurred during the double-blind phase of treatment, or within 1 day of stopping randomized treatment. Adverse events should not be included if they occurred prior to randomization or more than 1 day after discontinuing from randomized treatment. The end of trials with a tapering period should be set to be at the beginning of the tapering period. Events occurring more than 1 day after discontinuing from randomized treatment should be excluded even if discontinuation occurred before the nominal endpoint of the trial. For example, if a patient either discontinued of his own volition or was asked to discontinue by the investigator after 2 weeks of randomized treatment in a trial of 8 weeks duration, and the patient then experienced a "possibly suicide related" adverse event 2 days after stopping, that event should not be included.

Search Strategies for "Possibly Suicide-Related" Adverse Events

The following search strategies should be employed to identity adverse events of possible interest:

- Any events coded to preferred terms that include the text strings "suic" or "overdos," including all events coded as "accidental overdose" should be included.

- Regardless of the preferred term to which the verbatim term is mapped, all verbatim terms should be searched for the following text strings: "attempt", "cut", "gas", "hang", "hung", "jump", "mutilat-", "overdos-", "self damag-", "self harm", "self inflict", "self injur-", "shoot", "slash", "suic-", "poison", "asphyxiation", "suffocation", "firearm" should be included.

  Note: Any terms identified by this search because the text string was a substring of an unrelated word should be excluded (for example, the text string "cut" might identify the word "acute"). These terms might be characterized as "false positives" in the sense that the verbatim term was selected because one of the text strings occurred within that term but the term had no relevance to suicidality. Although we request that such terms be excluded, we ask that you prepare a table listing all such false positives, as follows:

Study #	Patient #	Treatment Assignment	Term in Which Text String Occurred

  The patients in this table will have as many rows as they have potential events.

- All deaths and other serious adverse events (SAEs) should be included.

- All adverse events coded as "accidental injury" should be included.

Preparation of Narrative Summaries for "Possibly Suicide-Related" Adverse Events

A complete set of narrative summaries should be prepared and collected for all "possibly suicide-related" adverse events. In some cases, narratives will have already been prepared, e.g., deaths and SAEs. In other cases, however, you will need to prepare narrative summaries by searching CRFs for any information that might be considered possibly relevant to suicidality. You should also utilize other relevant sources of information, e.g., hospital records, results of consults, questionnaire responses, etc, in preparing these narrative summaries. Depending on how much information is available, narrative summaries may be longer than 1 page, however, in no case, should more than 1 narrative summary be included on a single page. Following is the type of information that should be included in the original narrative summaries:

- Patient ID number
- Trial number
- Treatment group
- Dose at time of event (mg)
- Recent dose change – elaborate on timing and amount of dose change
- Sex
- Age
- Diagnosis
- History of suicidal thoughts
- History of suicide attempt
- History of self harm
- Adverse event Preferred term
- Adverse event Verbatim term
- Serious adverse event (y/n)
- Number of days on drug at time of event
- Treatment was discontinued following event (y/n)
- Patient had an emergency department visit and was discharged (y/n)
- Patient was hospitalized (y/n)
- Patient died (y/n) – if yes, elaborate on cause of death
- Associated treatment emergent adverse events
- Concurrent psychosocial stressors
- Psychiatric comorbidities
- Concomitant medications
    - Other pertinent information (e.g., family history of psychiatric disorders)-

Other relevant information for preparing narrative summaries:

-Patients may be identified as having events of interest in one or more of the above searches, and they may have more than one event of interest. In no case, however, should there be more than one narrative summary per patient. In cases where there is more than one event for a given patient, each different event should be clearly demarcated in the narrative.

-Only events occurring during the "exposure window" defined as during the double-blind phase (including the first day after abrupt discontinuation or the first day of taper, if tapering is utilized) should be included in the narrative summary, i.e., do not include any prerandomization events or events occurring more than 1 day after stopping randomized treatment or during the tapering period.
-Do not exclude events of interest on the basis of your judgment that they might not represent "treatment-emergent" events; we feel this judgment is too difficult to make and we prefer to simply include all potentially relevant events, regardless of whether or not similar thoughts or behaviors may have occurred prior to treatment.

Classification of "Possibly Suicide-Related" Adverse Events

Once the narrative summaries for "possibly suicide-related" adverse events are prepared and collected, we ask that you accomplish a rational classification of these events using the approach that was well-characterized by the Columbia group for the pediatric suicidality narratives. This approach was described in detail by Dr. Kelly Posner at the September 13 and 14, 2004 advisory committee meeting. The details are provided in her slides for that meeting (available on FDA's website), in the transcript for that meeting, and in other reviews, etc. pertinent to pediatric suicidality and available on FDA's website at the following URLs:

- Slides
  http://www.fda.gov/ohrms/dockets/ac/04/slides/2004-4065S1_06_FDA-Posner.ppt
- Briefing Document, transcripts, etc.
  http://www.fda.gov/ohrms/dockets/ac/cder04.html#PsychopharmacologicDrugs

The categories of interest from FDA's standpoint are as follows:

Suicide attempt (code 1)
Preparatory acts toward imminent suicidal behavior (code 2)
Self-injurious behavior, intent unknown (code 3)
Suicidal ideation (code 4)
Not enough information (code 5)
Self-injurious behavior, no suicidal intent (code 6)
Other: accident; psychiatric; medical (code 7)

Those individuals who classify the narratives must have the appropriate expertise and training to accomplish this task.

Prior to their rational classification, the narratives must be blinded to details that might bias their assessments. The details of appropriate blinding of the narratives can also be obtained in the transcript from the advisory committee meeting referred to above, and the materials available on FDA's website pertinent to that meeting. We request that you block out the following information that could reveal treatment assignment:

- Identifying patient information, identity of study drug, and patient's randomized drug assignment

- All identifying information regarding the sponsor, the clinical trial number, and the location of the trial
- All years with the exception of years in remote history
- Study drug start and stop dates (month, day, and year)
- All medications, both prescription and non-prescription, whether taken before, during, or after the study; non-pharmaceutical substances (e.g., alcohol, tobacco) should not be blocked out
- Names of medications involved in overdoses; the number of pills consumed should not be blocked out
- Indications for medications started during or after the study
- Indications for study drug

Once you have decided on an approach to accomplishing the task of blinding and classifying the narratives, we would be happy to review and comment on your plan.

Data Submission to DNDP

In order to perform additional analyses investigating the relationship between exposure to AEDs and "suicide-related" adverse events in adults and the pediatric population, we would appreciate your submitting the following variables as outlined in the next table. Note that we are requesting information from placebo (and "low dose-placebo") controlled trials only. We would expect that you will provide us with a completed JMP dataset within 6 months from the date of this letter.

Variable name	Type	Description	Coding notes
SOURCE	Character	First few letters of your drug name	
INDICATION	Character	Disease being studied in trial	E.g., epilepsy- adjunctive, epilepsy- monotherapy, bipolar disorder, migraine, etc.
TRIAL	Character	Trial ID	
CTPID	Character	Patient ID within each trial	
UNIQUEID	Character	A unique ID for every patient	Composed of "TRIAL" and "CTPID" joined in that order with no intervening punctuation or dashes
AGE	Numeric	Patient age	In years
AGECAT	Numeric	Age category	1=5-11 2=12-17 3=18-24 y 4=25-64 y 5=65 y or more
GENDER	Numeric	Patient gender	1=female 2=male

Variable name	Type	Description	Coding notes
RACE	Numeric	Patient race	1=White Caucasian 2=African-American 3=Hispanic 4=Asian 5=Other . = Missing
SETTING	Numeric	Setting of trial	1=inpatient 2=outpatient 3=both
LOCATION	Numeric	Location of trial	1=North America 2=Non-North America
TXARM	Numeric	Randomized treatment	1=drug 2=placebo 3=active control 4=low dose-placebo No missing values are allowed in this variable.
TXLOW	Character	Name of drug used as low dose-placebo	Leave patients in other treatment arms blank
TXACTIVE	Character	Name of drug used as active control	Leave patients in other treatment arms blank
EVENT	Numeric	This variable contains the code for the first suicidality event. If a patient had more than one event in the desired "exposure window", then the most severe event should be listed. Severity is decided based on the following order of codes 1>2>4>3>5	0=no event 1=suicide attempt 2=preparatory acts toward imminent suicidal behavior 3=self-injurious behavior, intent unknown 4=suicidal ideation 5=not enough information No missing values are allowed in this variable.
EVENTDAY	Numeric	The number of days to the first suicidal event counting from the day of the first dose.	for patients without events, this variable should contain days until end of trial or until premature discontinuation for patients with more than one event, this variable should contain days until the most severe event that is listed under the variable "EVENT"

Variable name	Type	Description	Coding notes
			No missing values are allowed in this variable.
DISCONT	Numeric	The patient discontinued before the end of the controlled portion of the trial	0=No 1=Yes No missing values are allowed in this variable

If you have questions, call Jacqueline H. Ware, Pharm.D., Senior Regulatory Project Manager, at (301) 594-5533.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Russell Katz
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